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(19) (CA) # CANADIAN PATENT

(54) 2-CARBALKOXY-AMINO-BENZIMIDAZOLE-5(6)-PHENYL ETHERS, PROCESS FOR THEIR MANUFACTURE AND THEIR USE IN ANTHELMINTICS

(72) Loewe, Heinz; Urbanietz, Josef; Kirsch, Reinhard and Düwel, Dieter, Germany (Federal Republic of)

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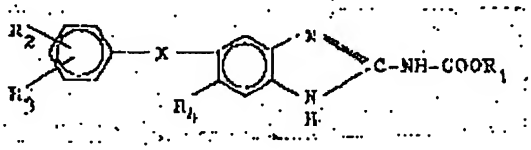
HOE 73/F 185

2-CARBALKOXY-AMINO-BENZIMIDAZOLE-5(6)-PHENYL ETHERS, PROCESS FOR THEIR MANUFACTURE AND THEIR USE IN ANTHELMINTICS

Abstract of the disclosure

A 2-carbalkoxy-amino-benzimidazole-5(6)-phenyl ether of the formula



in which R_1 represents an alkyl group having from 1 to 4 carbon atoms or a phenyl group; R_2 and R_3, which may be the same or different, each represents a hydrogen atom, a hydroxyl group, an alkoxy group having from 1 to 4 carbon atoms, a halogen atom, a trifluoromethyl group, an alkyl group having from 1 to 4 carbon atoms or a carbalkoxy group having from 1 to 4 carbon atoms in the alkoxy group, R_4 represents a hydrogen or chlorine atom and X represents oxygen or sulfur, which is prepared by converting a 2-amino-benzimidazole into an alkali metal or alkaline earth metal salt thereof and reacting it with a carbonate, suitable under exclusion of water, and then converting the carbonate salt, optionally by acidification, into free 2-benzimidazole carbamate of the formula (1).

The compounds have an anthelmintic activity.

Abstract Image

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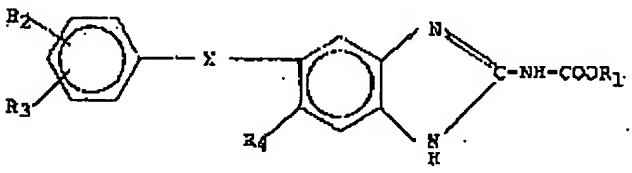
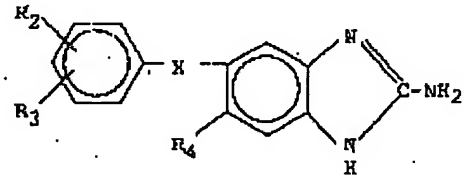
THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A process for the preparation of a 2-carbalkoxy-amino-benzimidazole-5(6)-phenyl ether of the formula I



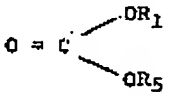
(I)

wherein R_1 represents an alkyl group having from 1 to 4 carbon atoms or a phenyl group; R_2 and R_3, which may be the same or different, each represents a hydrogen atom, a hydroxyl group, an alkoxy group having from 1 to 4 carbon atoms, a halogen atoms, a trifluoromethyl group, an alkyl group having from 1 to 4 carbon atoms or a carbalkoxy group having from 1 to 4 carbon atoms in the alkoxy group; R_4 represents a hydrogen or chlorine atom; and X represents oxygen or sulfur, in which a 2-amino-benzimidazole of the formula II



(II)

wherein R_2, R_3, R_4 and X are defined as above, is converted into an alkali metal or alkaline earth metal salt thereof, and the salt is reacted with a carbonate of the formula III



(III)

Claims Image

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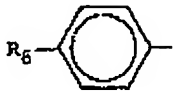
(4)

wherein R_1 and R_5, which may be the same or different, each represent an alkyl group of 1 to 4 carbon atoms or a phenyl group of the formula IV



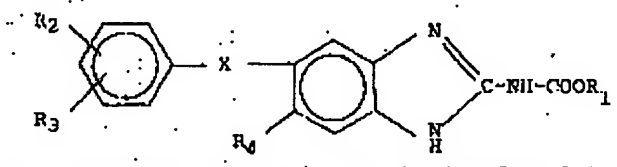
(IV)

wherein R_6 represents a hydrogen atom or the nitro atom, and the carbamate salt obtained is converted into the free 2-benzimidazole carbamate of the formula I, if desired.

2. A process as claimed in claim 1 in which the reaction is carried out in an inert organic solvent at a temperature of from 10 to 250°C.

3. A process as claimed in claim 2 in which the reaction is carried out at a temperature of from 25 to 100°C.

4. A 2-carbalkoxy-amino-benzimidazole-5(6)-phenyl ether of the formula I



(I)

wherein R_1 represents an alkyl group having from 1 to 4 carbon atoms or a phenyl group; R_2 and R_3, which may be the same or different, each represents a hydrogen atom, a hydroxyl group, an alkoxy group having from 1 to 4 carbon atoms, a halogen atom, a trifluoromethyl group, an alkyl group having from 1 to 4 carbon

(5)

atoms or a carbalkoxy group having from 1 to 4 carbon atoms in the alkoxy group; R_4 represents a hydrogen or chlorine atom; and X represents oxygen or sulfur, whenever obtained according to a process as claimed in claim 1, claim 2 or claim 3 or by an obvious chemical equivalent thereof.

5. A process as claimed in claim 1 for the preparation of 5-phenoxy-benzimidazole-2-methyl carbamate in which 2-amino-5-phenoxy-benzimidazole is converted into a salt by reaction with sodium methylate, the salt is reacted with dimethyl carbonate and the resultant carbamate salt is converted to the free 5-phenoxy-benzimidazole-2-methyl carbamate by treatment with hydrochloric acid.

6. 5-Phenoxy-benzimidazole-2-methyl carbamate whenever obtained according to a process as claimed in claim 5 or by an obvious chemical equivalent thereof.

7. A process as claimed in claim 1 for the preparation of 5-(3-chloro-phenoxy)-benzimidazole-2-methyl-carbamate in which 2-amino-5-(3-chloro-phenoxy)-benzimidazole is converted into a salt by treatment with sodium methylate, the salt is reacted with dimethyl carbonate and the resultant carbamate salt is converted to the free 5-(3-chloro-phenoxy)-benzimidazole-2-methyl-carbamate by treatment with hydrochloric acid.

8. 5-(3-Chloro-phenoxy)-benzimidazole-2-methyl-carbamate, whenever obtained according to a process as claimed in claim 7 or by an obvious chemical equivalent thereof.

9. A process as claimed in claim 1 for the preparation of

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5-(3-bromo-phenoxy)-benzimidazole-2-methyl-carbamate in which 2-amino-5-(3-bromo-phenoxy)-benzimidazole is converted into a salt by treatment with sodium methylate, the salt is reacted with dimethyl carbonate and the resultant carbamate salt is converted to the free 5-(3-bromo-phenoxy)-benzimidazole-2-methyl-carbamate by treatment with hydrochloric acid.

10. 5-(3-Bromo-phenoxy)-benzimidazole-2-methyl-carbamate, whenever obtained according to a process as claimed in claim 9 or by an obvious chemical equivalent thereof.

11. A process as claimed in claim 1 for the preparation of 5-(3-methyl-phenoxy)-benzimidazole-2-methyl-carbamate in which 2-amino-5-(3-methyl-phenoxy)-benzimidazole is converted into a salt by treatment with sodium methylate, the salt is reacted with dimethyl carbonate and the resultant carbamate salt is converted to the free 5-(3-methyl-phenoxy)-benzimidazole-2-methyl-carbamate by treatment with hydrochloric acid.

12. 5-(3-Methyl-phenoxy)-benzimidazole-2-methyl-carbamate, whenever obtained according to a process as claimed in claim 11 or by an obvious chemical equivalent thereof.

13. A process as claimed in claim 1 for the preparation of 5-(3-methoxy-phenoxy)-benzimidazole-2-methyl-carbamate in which 2-amino-5-(3-methoxy-phenoxy)-benzimidazole is converted into a salt by treatment with sodium methylate, the salt is reacted with dimethyl carbonate and the resultant carbamate salt is converted to the free 5-(3-methoxy-phenoxy)-benzimidazole-2-methyl-carbamate by treatment with hydrochloric acid.

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14. 5-(3-Methoxy-phenoxy)-benzimidazole-2-methyl-carbamate, whenever obtained according to a process as claimed in claim 13 or by an obvious chemical equivalent thereof.

15. A process as claimed in claim 1 for the preparation of 5-(3-chloro-phenoxy)-6-chloro-benzimidazole-2-methyl-carbamate in which 2-amino-5-(3-chloro-phenoxy)-6-chloro-benzimidazole is converted into a salt by treatment with sodium methylate, the salt is reacted with dimethyl carbonate and the resultant carbamate salt is converted to the free 5-(3-chloro-phenoxy)-6-chloro-benzimidazole-2-methyl-carbamate by treatment with hydrochloric acid.

16. 5-(3-Chloro-phenoxy)-6-chloro-benzimidazole-2-methyl-carbamate, whenever obtained according to a process as claimed in claim 15 or by an obvious chemical equivalent thereof.

17. A process as claimed in claim 1 for the preparation of 5-phenylthio-benzimidazole-2-methyl-carbamate in which 2-amino-5-phenylthio-benzimidazole is converted into a salt by treatment with sodium methylate, the salt is reacted with dimethyl carbonate and the resultant carbamate salt is converted to the free 5-phenylthio-benzimidazole-2-methyl-carbamate by treatment with hydrochloric acid.

18. 5-Phenylthio-benzimidazole-2-methyl-carbamate, whenever obtained according to a process as claimed in claim 17 or by an obvious chemical equivalent thereof.

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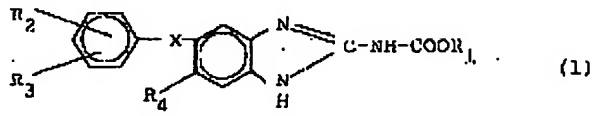
This invention relates to anthelmintically active benzimidazole derivatives, to a process for preparing them; to compositions containing them and to a method for combating helminths using them.

2-Carbalkoxy-amino-benzimidazole derivatives carrying alkyl or acyl groups in the 5(6) position are known to be anthelmintic agents (P. Actor et al., Nature 215, 321 (1967); DOS 2.029.637).

The present invention provides anthelmintically active 2-carbalkoxy-amino-benzimidazole-5(6)-phenyl ethers of the formula (1)



(1)

in which R_1 represents an alkyl group having from 1 to 4 carbon atoms or a phenyl group, R_2 and R_3, which may be the same or different, each represents a hydrogen atom, a hydroxyl group, an alkoxy group having from 1 to 4 carbon atoms, a halogen atom, a trifluoromethyl group, an alkyl group having from 1 to 4 carbon atoms or a carbalkoxy group having from 1 to 4 carbon atoms in the alkoxy group, R_4 represents a hydrogen or chlorine atom and X represents oxygen or sulfur.

Compounds of the formula (1) in which R_1 represents methyl, R_2 represents a hydrogen atom or a methyl group, R_3 and R_4 each represent hydrogen and X represents oxygen or sulfur are especially preferred.

The alkyl groups represented by R_1, R_2 and R_3 may be methyl, ethyl, propyl, isopropyl, butyl, sec.butyl and

Disclosures Image 1 of 12

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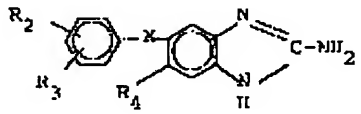
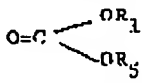
tert. butyl groups, moreover R_1 represents a phenyl group. The alkoxy groups represented by R_2 and R_3 may be methoxy, ethoxy, propoxy, isopropoxy and butoxy groups. The halogen atoms represented by R_2 and R_3 may be fluorine, chlorine, bromine and iodine atoms. The carbalkoxy groups represented by R_2 and R_3 may be carbomethoxy, carbethoxy, carbopropoxy and carbobutoxy groups.

The present invention also provides a process for the manufacture of 2-carbalkoxy-amino-benzimidazole-5(6)-phenyl ethers of the formula (1), in which R_1 to R_4 and X are defined as above, which comprises converting a 2-amino-benzimidazole of the formula (2)



(2)

in which R_2, R_3, R_4 and X are defined as in formula (1), into an alkali metal or alkaline earth metal salt thereof and reacting it with a carbonate of the formula (3)



(3)

in which R_1 and R_5 may be the same or different, each representing a lower alkyl group of 1 to 4 carbon atoms or a phenyl group of the formula (4)

(4)

in which R_6 represents a hydrogen atom or the nitro group, suitably under exclusion of water, and converting the carbamate

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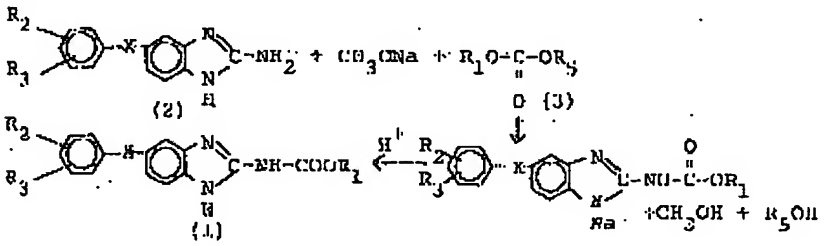
salt obtained, where required by acidification, into the free 2-benzimidazole carbamate of the formula (1).

In U.S. patent specification No. 3,480,642, it has been proposed to prepare 1-alkoxycarbonyl-2-aminobenzimidazoles from 2-amino-benzimidazole by reaction with chloroformlates and to rearrange these by heating them in anhydrous pyridine, dimethylformamide or acetonitrile, to yield 2-alkoxycarbonyl-amino-benzimidazoles. The rearrangement reaction, however, affords only very poor yields and gives mainly by-products which are insoluble in alkaline agents and acids, so that it is of no economic importance. Surprisingly, the reaction using carbonates gives excellent yields and no undesired 1-isomer.

The reaction may be illustrated by the following general scheme, sodium methylate being used as a base:



The novel 2-amino-benzimidazoles of the formula (2) used as starting material may be prepared according to known methods, for example disclosed in U.S. patent specification No. 3,455,948.

The carbonates required for the process of the invention are well known; dimethyl carbonate, dibutyl carbonate, methyl-phenyl carbonate, diphenyl carbonate and methyl-(p-nitrophenyl)

carbonate may be mentioned as examples.

The process of the invention may advantageously be carried out in an inert organic solvent, such as an alcohol of 1 to 4 carbon atoms, tetrahydrofuran, dioxan, acetonitrile, dimethylformamide, acetone, methyl-ethyl-ketone, diethyleneglycol dimethyl ether or in a carbonate of the formula (3) as a solvent. The 2-amino-benzimidazole or a correspondingly substituted derivative may first be converted into its salt which may then be used for the reaction. For such a salt formation, alkali metal and alkaline earth metal alcoholates and hydroxides are especially useful but also bases, for example $NaNH_2$ and NaH, as well as organo-metallic compounds, for example triphenyl sodium. The salt may, however, also be formed in situ and immediately processed in solution or suspension, but in this case anhydrous bases have to be used.

Generally, the base and the carbonate are added to the solution or suspension of the 2-amino-benzimidazole in an organic solvent, the succession of the reaction components added and the amount of the solvent being not critical. For economical reasons, it is advantageous to keep the reaction volume small. It is not necessary to use the reaction components of 2-amino-benzimidazole in equivalent proportions, the carbonate may rather be used in excess or as solvent and the base may also be used in an excess.

The reaction time ranges from a few minutes to several hours, and the reaction temperature is in the range of from 10° to 250° C, preferably from 25° to 100°C. The reaction yields a benzimidazole carbamate salt which is generally insoluble in the reaction medium. This salt may be isolated by filtration

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but it is also possible to obtain the free 2-benzimidazole carbamate by acidification. For this purpose, the pH-value of the reaction product is advantageously adjusted between 5 and 3 by means of an organic or inorganic acid, for example acetic acid, formic acid, hydrochloric acid or sulfuric acid. It is advantageous first to dilute the reaction product with water. Alternatively, the first isolated salt may also be suspended or dissolved in water and then adjusted to the desired pH-value.

The insoluble reaction product of the formula (I) is suction-filtered, washed and dried.

The 2-carbalkoxy-amino-benzimidazole-5(6)-phenyl ethers and thioethers of the present invention are valuable chemotherapeutic agents and are suitable for combating diseases caused by parasites in humans and animals.

They are particularly active against a great number of helminths, for example Haemonchus, Trichlostrongylus, Ostertagia, Strongyloides, Cooperia, Chabertia, Oesophagostomum, Hyostrongylus, Ankylostoma, Askaris and Heterakis. Particularly marked is the activity against gastro-intestinal Strongylides, which are above all infesting ruminants. The infestation of the animals by these parasites causes great economical damages, so that the compounds of the invention are mainly used in veterinary medicine.

The active substances according to the invention are administered together with suitable pharmaceutical solvents or carriers, perorally or subcutaneously, the one or the other form of administration being preferred in accordance with the prevailing circumstances.

The activity of the compounds of the invention was tested

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by chemotherapeutic experiments carried out on ewe-lambs having a weight of about 30 kg and which had been infested artificially with larvae of Haemonchus contortus or Trichostrongylus colubriformis. The test animals were kept in tiled stalls which were daily thoroughly cleaned. After termination of the prepatency period (time between infection and maturity of the parasites with beginning excretion of eggs or larvae), the number of eggs per gram of faeces was determined with the modified McMaster process according to Wetzel (Tierärztliche Umschau 6, 209 - 210 (1951)). Directly thereafter, the treatment of the sheep (in general 4 to 8 animals per active substance, at least however 2) was begun. The animals obtained perorally, in one case also subcutaneously, a suspension of 2.5 or 5 mg/kg of body weight in, each time, 10 ml of a 1 % Tylose (Registered Trade Mark) suspension. On the 7th, 14th and 28th day after the treatment, the number of eggs per gram of faeces was determined according to the above-indicated method and the percentage degree of decrease in comparison to the value determined before the beginning of the treatment was calculated.

The following Table indicates the activity of the new substances of the invention determined according to the above-described method in comparison to two known compounds of similar structure; these compounds were Parbendazol (cf. P. Actor et al., Nature 215, 321 (1967); D. Ross, Veterinary Record 82, 731 (1968); D. R. Johns et al., Australian Veterinarian Journal 45, 460 (1969) and Mebendazol (DOS 2.029.637).

The novel active substances of the invention were designated as follows:

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A = 5-phenoxy-benzimidazole-2-methyl-carbamate

B = 5-(4-chloro-phenoxy)-benzimidazole-2-methyl-carbamate

C = 5-(3-chloro-phenoxy)-benzimidazole-2-methyl-carbamate

D = 5-(2-chloro-phenoxy)-benzimidazole-2-methyl-carbamate

E = 5-(3-methoxy-phenoxy)-benzimidazole-2-methyl-carbamate

F = 5-phenylmercapto-benzimidazole-2-methyl-carbamate

The known active substances were designated as follows:

Comp. subst. 1 = Parbendazol

Comp. subst. 2 = Mebendazol

T A B L E

Active substance	Dos. cur. min. in mg/kg	Administration	Effect in %
A	2.5	peroral	100
B	5.0	peroral	94
C	2.5	peroral	100
D	5.0	peroral	96
E	2.5	peroral	100
F	2.5	peroral	100
F	2.5	subcutaneous	100
Comp. subst. 1	15.0	peroral	100
Comp. subst. 2	10.0	peroral	76 - 100

As the Table shows, the new carbamates of the invention are superior to known compounds of similar structure in that the Dosis curativa minima is essentially lower.

The Dosis tolerata maxima of the products of the invention is higher than 3200 mg/kg of body weight, upon peroral and subcutaneous administration.

The active substances of the formula I of the invention

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are administered, depending on the case, in doses ranging between 0.5 and 50 mg per kg of body weight for a period of 1 to 14 days.

For oral application, there may be used tablets, dragées, capsules, powders, granulates or pastes which contain the active substance together with the usual excipients and adjuvants such as starch, cellulose powder, talc, magnesium stearate, sugar, gelatin, calcium carbonate, finely distributed silicic acid, carboxymethyl cellulose and similar substances.

For parenteral administration, there may be used solutions, for example oily solutions, prepared using sesame oil, castor oil or synthetic triglycerides, optionally with the addition of tokopherol as anti-oxidation agent and/or using surface-active substances such as sorbitane fatty acid ester. In addition, there may be used aqueous suspensions prepared with the use of ethoxylated sorbitane fatty acid esters, optionally with the addition of thickening agents such as polyethylene glycol or carboxymethyl cellulose.

The concentrations of the active substances of the invention in the preparations prepared therewith are preferably in the range of from 2 to 20 % by weight; for the use as medicaments for humans, the concentrations of the active substances are preferably in the range of from 20 to 80 % by weight.

The following Examples illustrate the invention.

EXAMPLE 1:

5-Phenoxy-benzimidazole-2-methyl carbamate

41.5 Grams of 2-amino-5-phenoxy-benzimidazole were suspended in 300 ml of tetrahydrofuran, and 16.5 g of sodium

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methylate and 22.5 g of dimethyl carbonate were added. The mixture was refluxed for 2 hours. The suspension was then poured into 400 ml of water and neutralized by means of hydrochloric acid. The 5-phenoxy-benzimidazole-2-methyl carbamate formed was suction-filtered and recrystallized from glacial acetic acid/methanol.

Melting point: 248° C with decomposition.

In an analogous manner, the following compounds were prepared:

2. From 2-amino-5-(4-chloro-phenoxy)-benzimidazole the 5-(4-chloro-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 197°C.

3. From 2-amino-5-(3-chloro-phenoxy)-benzimidazole the 5-(3-chloro-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 230°C.

4. From 2-amino-5-(2-chloro-phenoxy)-benzimidazole, the 5-(2-chloro-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 206°C.

5. From 2-amino-5-(2,5-dichloro-phenoxy)-benzimidazole, the 5-(2,5-dichloro-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 244°C.

6. From 2-amino-5-(3,5-dichloro-phenoxy)-benzimidazole, the 5-(3,5-dichloro-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 226°C.

7. From 2-amino-5-(4-bromo-phenoxy)-benzimidazole, the 5-(4-bromo-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 248°C.

8. From 2-amino-5-(3-bromo-phenoxy) benzimidazole, the 5-(3-bromo-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 232°C.

9. From 2-amino-5-(3-bromo-phenoxy)-benzimidazole, the 5-(2-bromo-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 211°C.

10. From 2-amino-5-(4-methyl-phenoxy)-benzimidazole, the 5-(4-methyl-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 251°C.

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11. From 2-amino-5-(3-methyl-phenoxy)-benzimidazole, the 5-(3-methyl-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 228°C.

12. From 2-amino-5-(2-methyl-phenoxy)-benzimidazole, the 5-(2-methyl-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 216°C.

13. From 2-amino-5-(4-tert. butyl-phenoxy)-benzimidazole, the 5-(4-tert. butyl-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 250°C.

14. From 2-amino-5-(2,4-dimethyl-phenoxy)-benzimidazole, the 5-(2,4-dimethyl-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 239°C.

15. From 2-amino-5-(2-chloro-4-methyl-phenoxy)-benzimidazole, the 5-(2-chloro-4-methyl-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 209°C.

16. From 2-amino-5-(2-chloro-6-methyl-phenoxy)-benzimidazole, the 5-(2-chloro-6-methyl-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 300°C.

17. From 2-amino-5-(3-chloro-4-methyl-phenoxy)-benzimidazole, the 5-(3-chloro-4-methyl-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 236°C.

18. From 2-amino-5-(3-chloro-6-methyl-phenoxy)-benzimidazole, the 5-(3-chloro-6-methyl-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 218°C.

19. From 2-amino-5-(3-chloro-4-carbethoxy-phenoxy)-benzimidazole, the 5-(3-chloro-4-carbethoxy-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 194°C.

20. From 2-amino-5-(4-chloro-2-methyl-phenoxy)-benzimidazole, the 5-(4-chloro-2-methyl-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 230°C.

21. From 2-amino-5-(4-chloro-3-methyl-phenoxy)-benzimidazole, the 5-(4-chloro-3-methyl-phenoxy)-benzimidazole-2-methyl-

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carbamate, m.p. 253°C.

22. From 2-amino-5-(4-chloro-3,5-dimethyl-phenoxy)-benzimidazole, the 5-(4-chloro-3,5-dimethyl-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 239°C.

23. From 2-amino-5-(3,5-bis-trifluoromethyl-phenoxy)-benzimidazole, the 5-(3,5-bis-trifluoromethyl-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 238°C.

24. From 2-amino-5-(4-methoxy-phenoxy)-benzimidazole, the 5-(4-methoxy-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 246°C.

25. From 2-amino-5-(3-methoxy-phenoxy)-benzimidazole, the 5-(3-methoxy-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 203°C.

26. From 2-amino-5-(2-methoxy-phenoxy)-benzimidazole, the 5-(2-methoxy-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 212°C.

27. From 2-amino-5-(4-propoxy-phenoxy)-benzimidazole, the 5-(4-propoxy-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 218°C.

28. From 2-amino-5-(4-isopropoxy-phenoxy)-benzimidazole, the 5-(4-isopropoxy-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 208°C.

29. From 2-amino-5-(4-butoxy-phenoxy)-benzimidazole, the 5-(4-butoxy-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 210°C.

30. From 2-amino-5-(4-iso-butoxy-phenoxy)-benzimidazole, the 5-(4-iso-butoxy-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 198°C.

31. From 2-amino-5-phenoxy-6-chloro-benzimidazole, the 5-phenoxy-6-chloro-benzimidazole-2-methyl-carbamate, m.p. 270°C.

32. From 2-amino-5-(4-chloro-phenoxy)-6-chloro-benzimidazole, the 5-(4-chloro-phenoxy)-6-chloro-benzimidazole-2-methyl-carbamate, m.p. 305°C.

33. From 2-amino-5-(3-chloro-phenoxy)-6-chloro-benzimidazole,

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the 5-(3-chloro-phenoxy)-6-chloro-benzimidazole-2-methyl-carbamate, m.p. 263°C.

34. From 2-amino-5-(2-chloro-phenoxy)-6-chloro-benzimidazole, the 5-(2-chloro-phenoxy)-6-chloro-benzimidazole-2-methyl-carbamate, m.p. 238°C.

35. From 2-amino-5-(4-hydroxy-phenoxy)-benzimidazole, the 5-(4-hydroxy-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 238°C.

36. From 2-amino-5-(3-hydroxy-phenoxy)-benzimidazole, the 5-(3-hydroxy-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 197°C.

37. From 2-amino-5-(2-hydroxy-phenoxy)-benzimidazole, the 5-(2-hydroxy-phenoxy)-benzimidazole-2-methyl-carbamate, m.p. 223°C.

38. From 2-amino-5-phenylthio-benzimidazole, the 5-phenylthio-benzimidazole-2-methyl-carbamate, m.p. 233°C.

39. From 2-amino-5-phenoxy-benzimidazole with dibutyl carbamate, the 5-phenoxy-benzimidazole-2-butyl-carbamate, m.p. 180°C.

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Drawing
Image

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